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=> b reg;d que sta l8
FILE 'REGISTRY' ENTERED AT 09:02:44 ON 01 MAY 2007
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STRUCTURE FILE UPDATES:   30 APR 2007  HIGHEST RN 933825-30-0
DICTIONARY FILE UPDATES:  30 APR 2007  HIGHEST RN 933825-30-0

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

  Please note that search-term pricing does apply when
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experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

L6              STR
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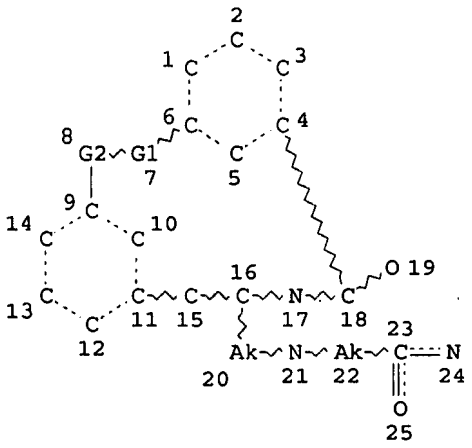


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VAR G1=O/CH2
REP G2=(3-3) CH2
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  25

STEREO ATTRIBUTES: NONE
L8            34 SEA FILE=REGISTRY SSS FUL L6

100.0% PROCESSED   63422 ITERATIONS                     34 ANSWERS
SEARCH TIME: 00.00.03


=> b hcap;d bib abs fhitstr hitrn retable l10 tot
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FILE 'HCAPLUS' ENTERED AT 09:03:12 ON 01 MAY 2007

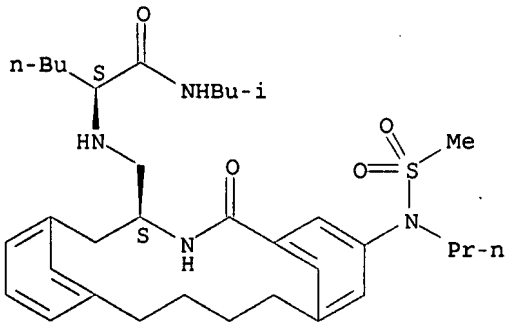

FILE COVERS 1907 - 1 May 2007 VOL 146 ISS 19
FILE LAST UPDATED: 30 Apr 2007 (20070430/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L10 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1149497 HCAPLUS
DN 146:19371
TI Macrocyclic Inhibitors of β-Secretase: Functional Activity in an Animal Model. [Erratum to document cited in CA145:465146]
AU Stachel, Shawn J.; Coburn, Craig A.; Sankaranarayanan, Sethu; Price, Eric A.; Wu, Guoxin; Crouthamel, Michelle; Pietrak, Beth L.; Huang, Qian; Lineberger, Janet; Espeseth, Amy S.; Jin, Lixia; Ellis, Joan; Holloway, M. Katharine; Munshi, Sanjeev; Allison, Timothy; Hazuda, Daria; Simon, Adam J.; Graham, Samuel L.; Vacca, Joseph P.
CS Department of Medicinal Chemistry, Biological Chemistry, Molecular Systems and Structural Biology, Merck Research Laboratories, West Point, PA, 19486, USA
SO Journal of Medicinal Chemistry (2006), 49(24), 7252
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB Guoxin Wu and Michelle Crouthamel were inadvertently omitted from the author list. Their affiliation is the Department of Biol. Chemical, represented by the double dagger symbol in the paper. The correct author list is given.
IT **847157-19-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macrocyclic inhibitors of β-secretase and functional activity in an animal model (Erratum))
RN 847157-19-1 HCAPLUS
CN Hexanamide, N-(2-methylpropyl)-2-[[[(4S)-17-[(methylsulfonyl)propylamino]-2-oxo-3-azatricyclo[13.3.1.16,10]eicosa-1(19),6,8,10(20),15,17-hexaen-4-yl]methyl]amino]-, (2S)- (CA INDEX NAME)

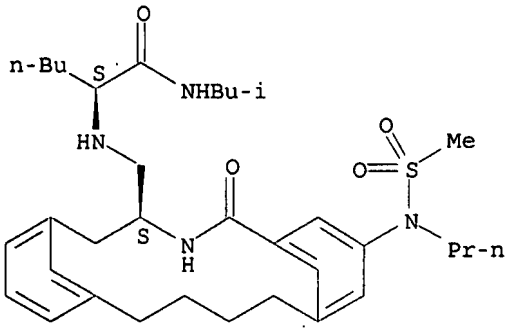
Absolute stereochemistry.



IT **847157-19-1P 847157-32-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macrocyclic inhibitors of β-secretase and functional activity in an animal model (Erratum))

L10 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:908572 HCAPLUS
DN 145:465146
TI Macrocyclic Inhibitors of β-Secretase: Functional Activity in an Animal Model
AU Stachel, Shawn J.; Coburn, Craig A.; Sankaranarayanan, Sethu; Price, Eric A.; Pietrak, Beth L.; Huang, Qian; Lineberger, Janet; Espeseth, Amy S.; Jin, Lixia; Ellis, Joan; Holloway, M. Katharine; Munshi, Sanjeev; Allison, Timothy; Hazuda, Daria; Simon, Adam J.; Graham, Samuel L.; Vacca, Joseph P.
CS Department of Medicinal Chemistry, Biological Chemistry, Molecular Systems and Structural Biology, Merck Research Laboratories, West Point, PA, 19486, USA
SO Journal of Medicinal Chemistry (2006), 49(21), 6147-6150
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB A macrocyclic inhibitor of β-secretase was designed by covalently crosslinking the P1 and P3 side chains of an isophthalamide-based inhibitor. Macrocyclization resulted in significantly improved potency and phys. properties when compared to the initial lead structures. More importantly, these macrocyclic inhibitors also displayed in vivo amyloid lowering when dosed in a murine model.
IT **847157-19-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macrocyclic inhibitors of β-secretase and functional activity in an animal model)
RN 847157-19-1 HCAPLUS
CN Hexanamide, N-(2-methylpropyl)-2-[[[(4S)-17-[(methylsulfonyl)propylamino]-2-oxo-3-azatricyclo[13.3.1.16,10]eicosa-1(19),6,8,10(20),15,17-hexaen-4-yl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.




IT **847157-19-1P 847157-32-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macrocyclic inhibitors of β-secretase and functional activity in an animal model)

RETABLE

| Referenced Author (RAU) | Year (RPY) | VOL (RVL) | PG (RPG) | Referenced Work (RWK) | Referenced File |
|---|---|---|---|---|---|
| Beher, D | 2005 | 14 | 1385 | Expert Opin Invest D | HCAPLUS |
| Best, B | 2005 | 313 | 902 | Pharmacol Exp Ther | |
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| Cai, H | 2001 | 4 | 233 | Nat Neurosci | HCAPLUS |
| Coburn, C | 2006 | 16 | 3635 | Bioorg Med Chem Lett | HCAPLUS |
| Goate, A | 1991 | 349 | 523 | Nature | |
| Hannessian, S | 2006 | 49 | 4544 | J Med Chem | |
| Hardy, J | 1997 | 349 | 704 | Proc Natl Acad Sci U | |
| Hu, X | 2004 | 47 | 4941 | J Med Chem | HCAPLUS |
| Lamb, B | 1993 | 5 | 22 | Nat Genet | HCAPLUS |
| Lamb, B | 1993 | 5 | 22 | Nature Genetics | HCAPLUS |
| Milano, J | 2004 | 82 | 341 | Toxicol Sci | HCAPLUS |
| Roberds, S | 2001 | 10 | 1317 | Hum Mol Genet | HCAPLUS |
| Rojo, I | 2006 | 16 | 191 | Bioorg Med Chem Lett | HCAPLUS |
| Sankaranarayanan, S | 2006 | | | 10th International c | |
| Savage, M | 1998 | 18 | 1743 | J Neurosci | HCAPLUS |
| Scholl, M | 1999 | 1 | 953 | Org Lett | HCAPLUS |
| Searfoss, G | 2003 | 278 | 46107 | J Biol Chem | HCAPLUS |
| Selkoe, D | 1996 | 271 | 18295 | J Biol Chem | HCAPLUS |
| Selkoe, D | 1999 | 399A | 23 | Nature | |
| Simon, A | 2005 | | | 2005 AD/PD meeting | |
| Sinha, S | 1999 | 96 | 11049 | Proc Natl Acad Sci U | HCAPLUS |
| Stachel, S | 2006 | 16 | 641 | Bioorg Med Chem Lett | HCAPLUS |
| Stachel, S | 2004 | 47 | 6117 | J Med Chem | |
| Stachel, S | 2004 | 47 | 6447 | J Med Chem | HCAPLUS |
| Thompson, L | 2005 | 11 | 3383 | Curr Pharm Des | HCAPLUS |
| Tilley, J | 1991 | 34 | 1125 | J Med Chem | HCAPLUS |
| Tsantrizos, Y | 2003 | 42 | 1356 | Angew Chem, Int Ed | HCAPLUS |

L10 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:177829 HCAPLUS
DN 142:280070
TI Preparation of macrocyclic β-secretase inhibitors for the treatment of Alzheimer's disease
IN Coburn, Craig; Stachel, Shawn J.; Vacca, Joseph P.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO2005018545 | A2 | 20050303 | 2004WO-US25791 | 20040810 |
| | WO2005018545 | A3 | 20050519 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | AU2004266605 | A1 | 20050303 | 2004AU-0266605 | 20040810 |
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| | EP---1656359 | A2 | 20060517 | 2004EP-0780598 | 20040810 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| | CN---1835936 | A | 20060920 | CN 2004-80023327 | 20040810 |
| | JP2007502278 | T | 20070208 | 2006JP-0523290 | 20040810 |
| | US2007037784 | A1 | 20070215 | 2006US-0568153 | 20060213 |
| PRAI | 2003US-495667P | P | 20030814 | | |
| | 2004WO-US25791 | W | 20040810 | | |

OS CASREACT 142:280070; MARPAT 142:280070

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Macrocyclic compds. of formula I [R1 = H, R4-S(O)pN(R5), CN, etc.; R2, R3 = H, alkyl, halo, OH, alkoxy, etc.; R4 = alkyl, (substituted) NH2, Ph, benzyl, etc.; R5 = H, alkyl, Ph, benzyl; p = 0-2; X = CH2, O] are prepared which are inhibitors of the β-secretase enzyme and that are useful in the treatment or prevention of diseases such as Alzheimer's disease. The invention is also directed to pharmaceutical compns. comprising these compds. and the use of these compds. and compns. in the prevention or treatment of such diseases in which the β-secretase enzyme is involved. Thus, II was prepared from Me 3-nitrobenzoate, allyltributyl stannane, m-allyltyrosine Me ester hydrochloride and N-isobutyl-L-norleucineamide hydrochloride in several steps. The compds. had IC50 from about 1 nM to 1 μM against β-secretase enzyme.

IT **847157-12-4P**

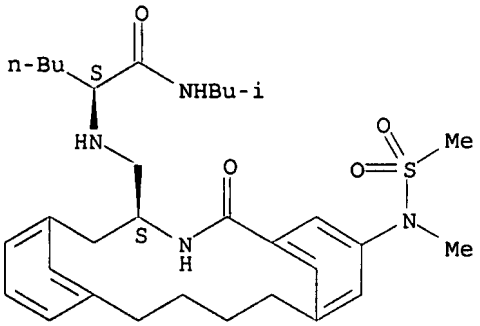
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of macrocyclic β-secretase inhibitors for treatment of Alzheimer's disease)

RN 847157-12-4 HCAPLUS

CN Hexanamide, 2-[[[(4S)-17-[methyl(methylsulfonyl)amino]-2-oxo-3-azatricyclo[13.3.1.16,10]eicosa-1(19),6,8,10(20),15,17-hexaen-4-yl]methyl]amino]-N-(2-methylpropyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




IT **847157-12-4P 847157-13-5P 847157-14-6P**
**847157-15-7P 847157-16-8P 847157-17-9P**
**847157-18-0P 847157-19-1P 847157-20-4P**
**847157-21-5P 847157-22-6P 847157-23-7P**
**847157-24-8P 847157-25-9P 847157-26-0P**
**847157-28-2P 847157-30-6P 847157-31-7P**
**847157-32-8P 847157-33-9P 847157-34-0P**
**847157-35-1P 847157-36-2P 847157-37-3P**
**847157-38-4P 847157-39-5P 847157-40-8P**
**847157-41-9P 847157-42-0P 847157-43-1P**
**847157-44-2P 847157-45-3P 847157-46-4P**
**847225-40-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of macrocyclic β-secretase inhibitors for treatment of Alzheimer's disease)

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FILE LAST UPDATED: 26 APR 2007 <20070426/UP>
MOST RECENT THOMSON SCIENTIFIC UPDATE: 200727 <200727/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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http://www.stn-international.de/archive/stn_online_news/fraghitstr_ex.pdf

>>> IPC Reform backfile reclassification has been loaded to 31 December 2006. No update date (UP) has been created for the reclassified documents, but they can be identified by 20060101/UPIC and 20061231/UPIC. <<<

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http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf

>>> FOR DETAILS ON THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX
PLEASE SEE
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<
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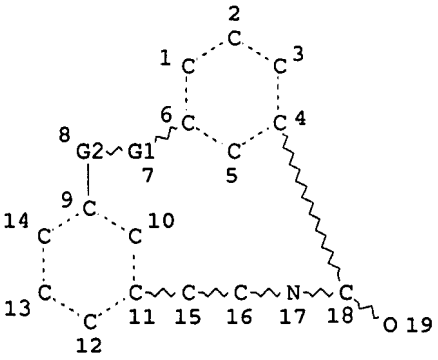
L1 STR




VAR G1=O/CH2
REP G2=(3-3) CH2
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE
L17 32 SEA FILE=WPIX SSS FUL L1

100.0% PROCESSED 9531 ITERATIONS 32 ANSWERS
SEARCH TIME: 00.00.07

=> d bib abs dcn l20 tot

L20 ANSWER 1 OF 1 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
AN 2005-202434 [21] WPIX
DNC C2005-064723 [21]
TI New 3-aza-tricyclo-icosa-hexaene derivatives useful as macrocyclic beta-secretase inhibitor for treating Alzheimer's disease
DC B02
IN COBURN C; STACHEL S; STACHEL S J; VACCA J; VACCA J P; COBURN C A
PA (MERI-C) MERCK & CO INC; (COBU-I) COBURN C A; (STAC-I) STACHEL S J; (VACC-I) VACCA J P
CYC 107
PIA WO--2005018545 A2 20050303 (200521)* EN 42[0]
EP-----1656359 A2 20060517 (200634) EN
AU--2004266605 A1 20050303 (200663) EN
CN-----1835936 A 20060920 (200706) ZH
JP--2007502278 W 20070208 (200713) JA 38
US-20070037784 A1 20070215 (200715) EN
ADT WO--2005018545 A2 2004WO-US0025791 20040810; AU--2004266605 A1 2004AU-000266605 20040810; CN-----1835936 A 2004CN-080023327 20040810; EP-----1656359 A2 2004EP-000780598 20040810; EP-----1656359 A2 2004WO-US0025791 20040810; JP--2007502278 W 2004WO-US0025791 20040810; JP--2007502278 W 2006JP-000523290 20040810; US-20070037784 A1 Provisional

2003US-000495667P 20030814; US-20070037784 A1 2004WO-US0025791 20040810; US-20070037784 A1 2006US-000568153 20060213

FDT EP-----1656359 A2 Based on WO--2005018545 A; AU--2004266605 A1 Based on WO--2005018545 A; JP--2007502278 W Based on WO--2005018545 A

PRAI 2003US-000495667P 20030814
2006US-000568153 20060213

AN 2005-202434 [21] WPIX

AB WO 2005018545 A2 UPAB: 20060121

NOVELTY - 3-Aza-tricyclo-icosa-hexaene derivatives are new.

DETAILED DESCRIPTION - 3-Aza-tricyclo-icosa-hexaene derivatives of formula (I) are new.

R1 = H, R4S(O)pN(R5), CN, 1-6C alkyl-CN, halo, phenyl (optionally mono- - penta-substituted with CN, halo, 1-6C alkyl, OR5, CO2R5 or C(O)R5 or group of formula (i);

R4 = 1-8C alkyl (optionally substituted 1 to 7 times by F), NR5R6, phenyl or benzyl;

R5 and R6 = H, 1-6C alkyl (optionally mono- - hexa-substituted with F), phenyl or benzyl;

p = 0 - 2;

R2 = 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-8C cycloalkyl (all optionally substituted 1 to 7 times with halo, hydroxy, O-1-6C alkyl, 3-6C cycloalkyl, S(O)p-1-6C alkyl, CN, CO2H, CO2-1-6C alkyl, CO-NR5R6) or phenyl (optionally substituted 1 to 5 times with T), H or phenyl (optionally mono- - penta-substituted with T);

T = 1-6C alkyl, CN, halo, CF3, O-R5 or CO2R5);

R3 = H, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-8C cycloalkyl (all optionally substituted 1 to 7 times halo, hydroxy, trifluoromethyl, O-R5, CO2R5 , S(O)pN(R5)-1-6C alkyl, S(O)pN(R5)-phenyl, phenyl, pyridyl (both optionally substituted 1 to 5 times with T), phenyl (optionally mono- - penta-substituted by T);

X = CH2 or O.

ACTIVITY - Nootropic; Neuroprotective; Hemostatic; Cerebroprotective; Vulnerary; Vasotropic; Antiinflammatory; Antidiabetic; Antiarteriosclerotic.

MECHANISM OF ACTION - beta-Secretase activity inhibitor. The inhibitory activity of (I) is confirmed by HPLC assay. (I) Showed IC50 of 1 nM - 1 muM.

USE - For treating Alzheimer's disease (claimed); for treating diseases mediated by abnormal cleavage of amyloid precursor protein e.g. Cognitive impairment, Trisomy 21 (Down syndrome), cerebral amyloid angiopathy, degenerative dementia, hereditary cerebral hemorrhage with Amyloidosis of Dutch-Type, Creutzfeldt-Jakob disease, prion disorders, amyotrophic lateral sclerosis, progressive supranuclear palsy, head trauma, stoke, pancreatitis, inclusion body myositis, other peripheral amyloidosis, diabetes and atherosclerosis.

ADVANTAGE - The compound inhibits the activity of beta-secretase or BACE thus preventing the formation of insoluble Abeta and arresting the production of Abeta.

CMC M2 *01* DCN: **RAH7RT-N RAH7RT-T**
M2 *02* DCN: **RAH7RS-N RAH7RS-T**
M2 *03* DCN: **RAH7RR-N RAH7RR-T**
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M2 *05* DCN: **RAH7RP-N RAH7RP-T**
M2 *06* DCN: **RAH7RO-N RAH7RO-T**
M2 *07* DCN: **RAH7RN-N RAH7RN-T**
M2 *08* DCN: **RAH7RM-N RAH7RM-T**
M2 *09* DCN: **RAH7RL-N RAH7RL-T**
M2 *10* DCN: **RAH7RK-N RAH7RK-T**
M2 *11* DCN: **RAH7RJ-N RAH7RJ-T**
M2 *12* DCN: **RAH7RI-N RAH7RI-T**
M2 *13* DCN: **RAH7RH-N RAH7RH-T**
M2 *14* DCN: **RAH7RG-N RAH7RG-T**
M2 *15* DCN: **RAH7RF-N RAH7RF-T**
M2 *16* DCN: **RAH7RE-N RAH7RE-T**
M2 *17* DCN: **RAH7RD-N RAH7RD-T**
M2 *18* DCN: **RAH7RC-N RAH7RC-T**

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     M2 *25*    DCN: RAH7R5-N RAH7R5-T
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     M2 *28*    DCN: RAH7R2-N RAH7R2-T
     M2 *29*    DCN: RAH7R0-N RAH7R0-T
     M2 *30*    DCN: RAH7QZ-N RAH7QZ-T
     M2 *31*    DCN: RAH7QY-N RAH7QY-T
     M2 *32*    DCN: RAH7QX-N RAH7QX-T
     M2 *33*

=> d his

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     FILE 'REGISTRY' ENTERED AT 08:45:04 ON 01 MAY 2007
L1              STR

     FILE 'REGISTRY' ENTERED AT 08:49:07 ON 01 MAY 2007

     FILE 'HCAPLUS' ENTERED AT 08:49:11 ON 01 MAY 2007
L2            1 US20070037784/PN OR (US2006-568153 OR WO2004-US25791 OR US2003-

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L4            63 SEA L3
L5            38 L4 AND NR>=3
L6               STR L1
L7             1 L6
L8            34 L6 FULL
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L9            34 L8 AND L4

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L14            0 L8

     FILE 'BIOSIS' ENTERED AT 08:58:38 ON 01 MAY 2007
L15            0 L8

     FILE 'WPIX' ENTERED AT 08:59:12 ON 01 MAY 2007
L16            2 L1
L17           32 L1 FULL
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                 EDIT /DSCE
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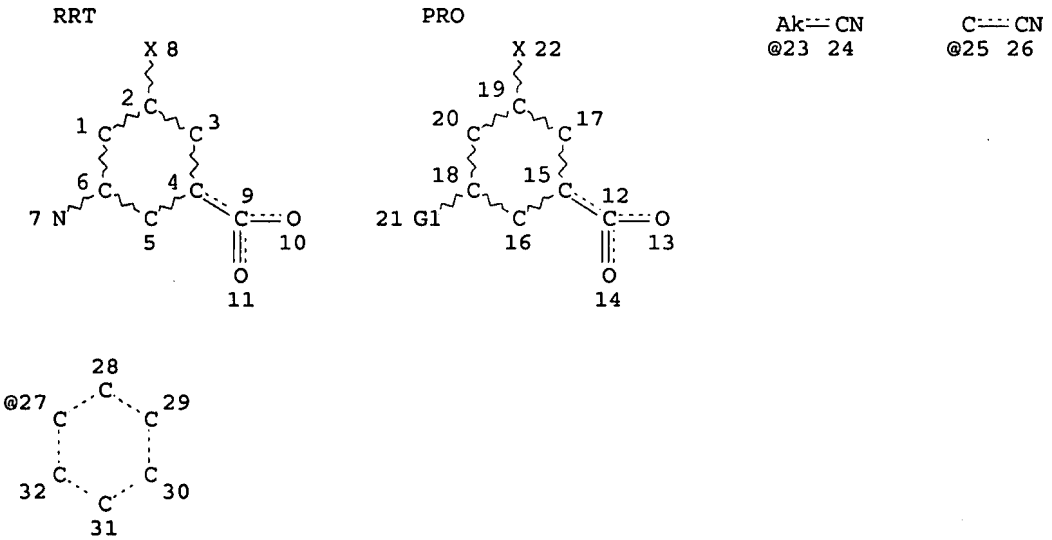


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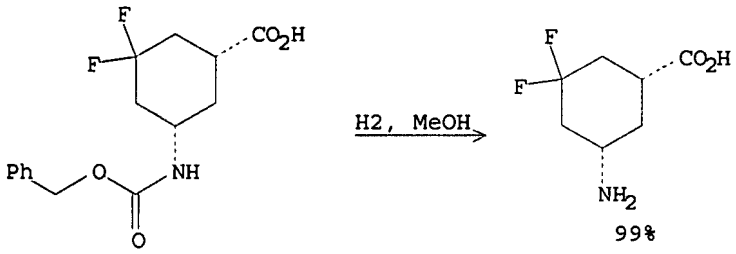
L3 ANSWER 1 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 144:381778 CASREACT
TI Syntheses and evaluation of fluorinated conformationally restricted analogues of GABA as potential inhibitors of GABA aminotransferase
AU Wang, Zhiyong; Silverman, Richard B.
CS Department of Chemistry, Department of Biochemistry, Molecular Biology, and Cell Biology, and the Center for Drug Discovery and Chemical Biology, Northwestern University, Evanston, IL, 60208-3113, USA
SO Bioorganic & Medicinal Chemistry (2006), 14(7), 2242-2252
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier B.V.
DT Journal
LA English
AB Inhibition of γ-aminobutyric acid aminotransferase (GABA-AT) could raise the concentration of GABA, an inhibitory neurotransmitter in the human brain, and could have therapeutic applications for a variety of neurol. diseases including epilepsy. Four fluorine-containing analogs of GABA with conformations restricted by a cyclohexane ring system were designed and synthesized, but unlike some of their five-membered ring counterparts, minimal inhibition of GABA-AT was observed It is likely that the rigid chair conformation of these compds. cannot be accommodated well in the enzyme's active site.

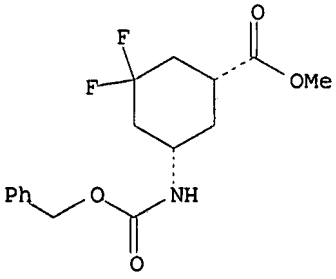
RX(2) OF 78




99%

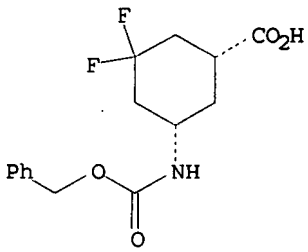
CON: overnight, room temperature

RX(14) OF 78



1. LiOH, Water, THF
2. HCl, Water

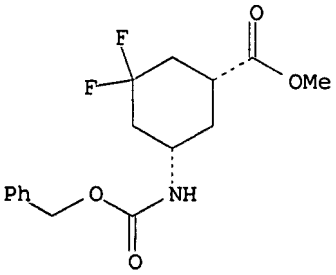
(step 1)



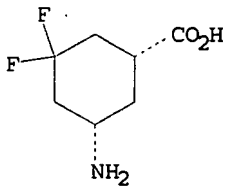
52%

CON: STAGE(1) overnight, room temperature
STAGE(2) room temperature, pH 1

RX(31) OF 78 - 2 STEPS



1.1. LiOH, Water, THF
1.2. HCl, Water
2. H2, MeOH



99%

CON: STEP(1.1) overnight, room temperature
STEP(1.2) room temperature, pH 1
STEP(2) overnight, room temperature

RETABLE

| Referenced Author (RAU) | Year (RPY) | VOL (RVL) | PG (RPG) | Referenced Work (RWK) | Referenced File |
|---|---|---|---|---|---|

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| Neal, M | 1977 | 138 | 169 | Brain Res | CAPLUS |
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| Osby, J | 1984 | 25 | 2093 | Tetrahedron Lett | CAPLUS |
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| Qiu, J | 1999 | 42 | 4725 | J Med Chem | CAPLUS |
| Qiu, J | 2000 | 43 | 706 | J Med Chem | CAPLUS |
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| Scott, E | 1958 | 234 | 932 | J Biol Chem | |
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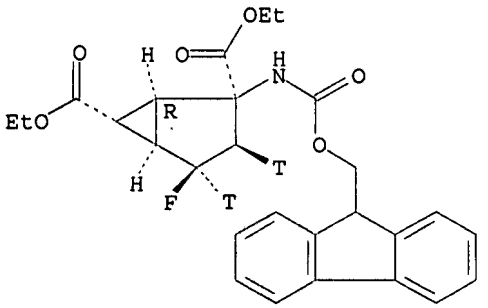
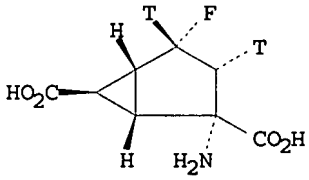
| Storici, P | 1999 | 38 | 8628 | Biochemistry | CAPLUS |
| Storici, P | 2004 | 43 | 14057 | Biochemistry | CAPLUS |
| Sugase, K | 2004 | 47 | 489 | J Med Chem | CAPLUS |
| Tian, F | 2000 | 2 | 563 | Org Lett | CAPLUS |
| Ye, Q | 2002 | 67 | 9288 | J Org Chem | CAPLUS |

L3 ANSWER 2 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 143:97106 CASREACT
TI 1. Synthesis of LY455169-[2H2], a model study for the tritium labeling of LY459477. 2. Synthesis of LY459477-[3H2]
AU Kuo, Fengjiun; Kulanthaivel, Palaniappan; Rener, Gregory A.; Wheeler, William J.; Yi, Ping
CS Lilly Research Laboratories, A Division of Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN, 46285, USA
SO Synthesis and Applications of Isotopically Labelled Compounds, Proceedings of the International Symposium, 8th, Boston, MA, United States, June 1-5, 2003 (2004), Meeting Date 2003, 267-270. Editor(s): Dean, Dennis C.; Filer, Crist N.; McCarthy, Keith E. Publisher: John Wiley & Sons Ltd., Chichester, UK.
CODEN: 69FZAZ; ISBN: 0-470-86365-X
DT Conference
LA English
AB LY459477 is a potent mGluR agonist. Tritiated material was required for use in receptor binding assays. To support in vitro receptor binding studies, a tritium labeled isotopomer with a high specific activity (over 20 Ci/mmol) was required. The key to the tritiation of LY459477 was to find a method for the incorporation of tritium into protected LY455169. A general and simple method was developed for the synthesis of a double deuterium (or tritium) labeled alc. from the corresponding ketone. The preparation of LY459477-[3H] was accomplished by following the conditions developed in model studies.

RX(10) OF 28



1. Et2NH, Dioxane
2. NaOH
3. HCl



(step 1)

NOTE: no exptl. detail

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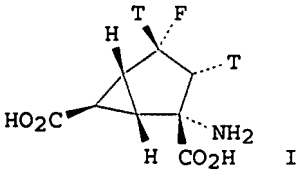
|---|---|---|---|---|---|
| Brown, H | 1963 | | 242 | Hydroboration | |
| Djerassi, C | 1948 | 70 | 417 | J Am Chem Soc | CAPLUS |
| Fieser | | 1 | 1050 | Reagents for Organic | |
| Fieser, L | 1953 | 75 | 1700 | J Am Chem Soc | CAPLUS |
| Goto, T | 1961 | | 513 | Tetrahedron Lett | |
| Henbest, H | 1955 | | 2477 | J Chem Soc | CAPLUS |
| Massey, S | 1998 | | 35 | Eur Pat Appl, EP 878 | |
| Sarma, J | 1985 | | 4657 | Tetrahedron Lett | |
| Schenker, E | 1961 | 73 | 81 | Anger Chem | CAPLUS |

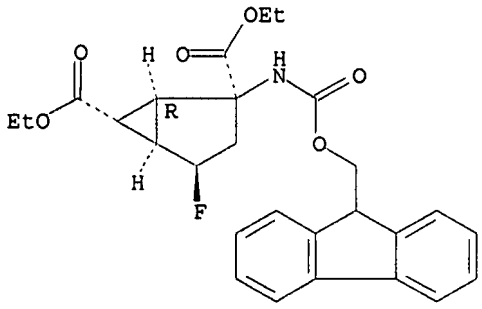
L3 ANSWER 3 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 142:240112 CASREACT
TI A method for the synthesis of 2-amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid-[3H2]
AU Kuo, Fengjiun; Kulanthaivel, Palaniappan; Rener, Gregory A.; Yi, Ping; Wheeler, William J.
CS Lilly Research Laboratories, A Division of Eli Lilly and Company Lilly Corporate Center, Indianapolis, IN, 46285, USA
SO Journal of Labelled Compounds & Radiopharmaceuticals (2004), 47(9), 571-581
CODEN: JLCRD4; ISSN: 0362-4803
PB John Wiley & Sons Ltd.
DT Journal
LA English
GI




I

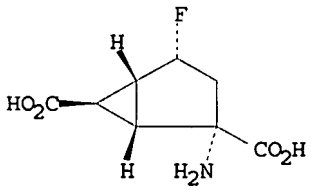
AB A process for double deuterium labeling of an alc. was developed. The process was utilized in the subsequent tritium labeling of a secondary alc. with high specific activity (24 Ci/mmol) by reduction of the corresponding ketone using sodium borotritide. The starting ketone was first brominated with pyridinium tribromide; the resulting alpha bromoketone was then reduced in THF/alc. in the presence of Ni(OAc)2. The alc. was then converted to dicarboxylic acid I, an mGluR agonist.

RX(7) OF 40



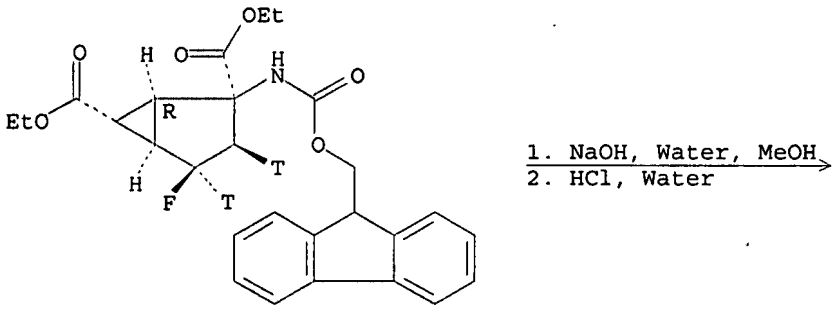

(step 1)

1. Et2NH, Dioxane
2. NaOH, Water, Dioxane
3. HCl, Water




CON: STAGE(1) overnight, room temperature
STAGE(2) overnight, room temperature
STAGE(3) room temperature

RX(10) OF 40

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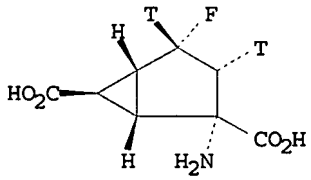


CON: STAGE(1) overnight, room temperature
STAGE(2) room temperature

RETABLE

| Referenced Author (RAU) | Year (RPY) | VOL (RVL) | PG (RPG) | Referenced Work (RWK) | Referenced File |
|---|---|---|---|---|---|
| Brown, H | 1963 | | 242 | Hydroboration | |
| Djerassi, C | 1948 | 70 | 417 | J Am Chem Soc | CAPLUS |
| Fieser, L | 1953 | 75 | 1700 | J Am Chem Soc | CAPLUS |
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| Goto, T | 1961 | 2 | 513 | Tetrahedron Lett | |
| Henbest, H | 1955 | | 2477 | J Chem Soc | CAPLUS |
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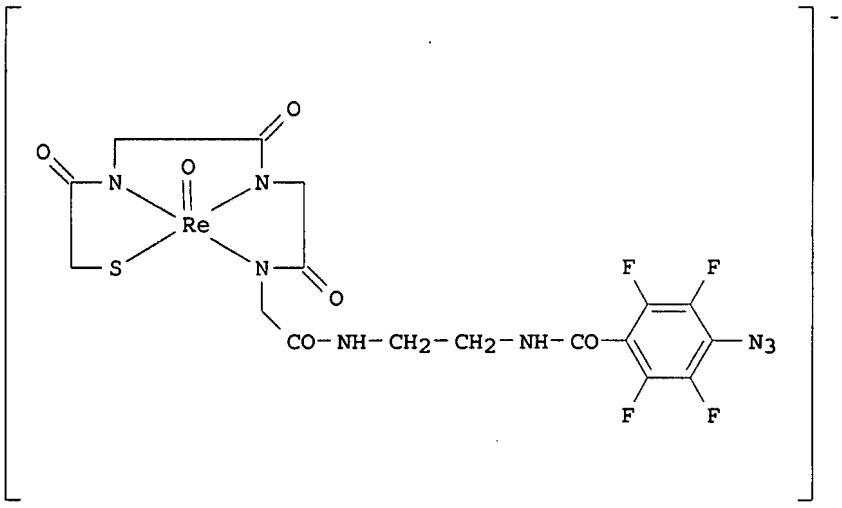
| Mikami, K | 1997 | 38 | 579 | Tetrahedron Lett | CAPLUS |
| Sarma, J | 1985 | 26 | 4657 | Tetrahedron Lett | CAPLUS |
| Schenker, E | 1961 | 73 | 81 | Anger Chem | CAPLUS |

L3 ANSWER 4 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 137:325389 CASREACT
TI Chemistry of Bifunctional Photoprobes. 6. Synthesis and Characterization of High Specific Activity Metalated Photochemical Probes: Development of Novel Rhenium Photoconjugates of Human Serum Albumin and Fab Fragments
AU Rajagopalan, Raghavan; Kuntz, Robert R.; Sharma, Uday; Volkert, Wynn A.; Pandurangi, Raghoottama S.
CS Department of Chemistry, University of Missouri, Columbia, MO, 65211, USA
SO Journal of Organic Chemistry (2002), 67(19), 6748-6757
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
GI



AB Functionalization of perfluoro aryl azides by bifunctional chelating agents (BFCAs) capable of forming high specific activity complexes with 99mTc (for γ-imaging) and 188Re (for radiotherapy) is described. The synthesis of multidonor BFCAs containing N2S2, N4, and N3S donor groups containing imidazole, pyridine, and pyrazine functionalities that may be important for tuning the pharmacokinetic parameters is also described. Functionalization of perfluoro aryl azides at various sites on BFCAs yields novel bifunctional photolabile chelating agents (BFPCAs) that are useful for covalent attachment to biomols. A representative Re-BFPCA I as the Me4N+ salt in a model solvent, diethylamine, proceeded to give a high yield of intermol. NH insertion product without the decomplexation of the metal ion from I. All products originated from the photolysis of I in diethylamine were characterized by anal. techniques, and a plausible mechanism of formation of different photolytic products is suggested. The high yield of intermol. NH insertion of I is extended to labeling of human serum albumin (HSA) and Fab fragments under aqueous conditions. The photolabeling technol. developed here offers a new way to attach diagnostically and therapeutically useful radiotracers (e.g., 99mTc, 188Re) to Fab fragments for potential noninvasive imaging and therapy of cancer.

RX(17) OF 59 - REACTION DIAGRAM NOT AVAILABLE
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|---|---|---|---|---|---|
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| Amato, R | 2000 | 126 | 161 | Cancer Res Clin Onco | CAPLUS |
| Arano, Y | 1999 | 59 | 128 | Cancer Res | CAPLUS |
| Baldas, J | 1999 | 41 | 1 | Advances in Inorgani | |
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| Bridger, G | 1996 | 7 | 255 | Bioconjugate Chem | CAPLUS |
| Bryson, N | 1990 | 29 | 2948 | Inorg Chem | CAPLUS |
| Cai, S | 1992 | 57 | 1299 | J Org Chem | CAPLUS |
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| Cesati, R | 2001 | 123 | 4093 | J Am Chem Soc | CAPLUS |
| Das, T | 2000 | 27 | 189 | Nucl Med Biol | CAPLUS |
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|---|---|---|---|---|---|
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| Kasina, S | 1991 | 32 | 1445 | J Nucl Med | CAPLUS |
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| Law, K | 1990 | 10 | 845 | Anticancer Res | CAPLUS |
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| Pandurangi, R | 1995 | | 565 | J Chem Soc, Dalton T | CAPLUS |
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| Schmidt, P | 1998 | 25 | 639 | Nucl Med Biol | CAPLUS |
| Schubiger, P | 1996 | 7 | 165 | Bioconjugate Chem | CAPLUS |
| Scott, E | 1997 | 8 | 146 | Bioconjugate Chem | |

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| Skaddan, M | 1999 | 64 | 8108 | J Org Chem | CAPLUS |
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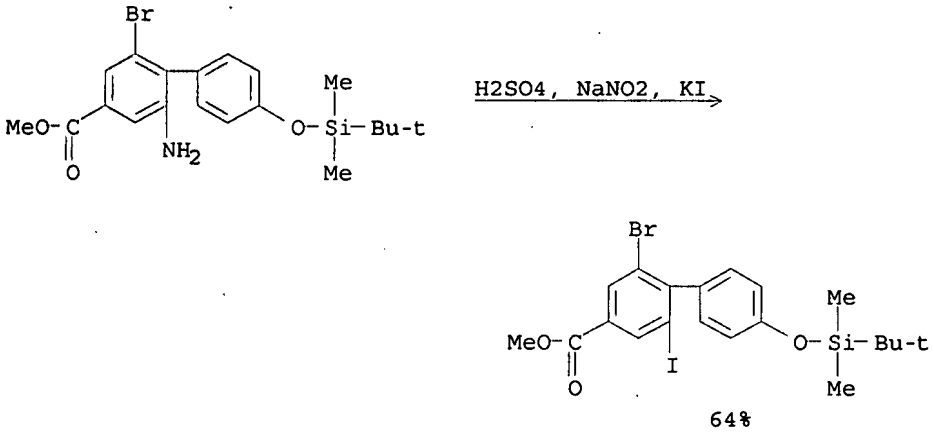
| Sugiyura, Y | 1978 | 17 | 2176 | Inorg Chem | |
| Tsai, S | 2001 | 12 | 264 | Bioconjugate Chem | CAPLUS |
| Ultee, M | 1997 | 38 | 133 | J Nucl Med | CAPLUS |
| Vangog, F | 1996 | 37 | 352 | J Nucl Med | CAPLUS |
| Volkert, W | 1999 | 99 | 2269 | Chem Rev | CAPLUS |
| Volkert, W | 1996 | | 123 | Topics in Current Ch | CAPLUS |
| Wilber, D | 1992 | 3 | 433 | Bioconjugate Chem | |
| Wust, F | 1999 | 7 | 1827 | Bioorg Med Chem | CAPLUS |
| Wust, F | 1998 | 63 | 665 | Steroids | CAPLUS |
| Yamamura, N | 1999 | 10 | 489 | Bioconjugate Chem | CAPLUS |

L3 ANSWER 5 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 135:257002 CASREACT
TI Biphenyls as surrogates of the steroidal backbone. Part 1. Synthesis and estrogen receptor affinity of an original series of polysubstituted biphenyls
AU Lesuisse, D.; Albert, E.; Bouchoux, F.; Cerede, E.; Lefrancois, J.-M.; Levif, M.-O.; Tessier, S.; Tric, B.; Teutsch, G.
CS Medicinal Chemistry, Aventis, Romainville, 93235, Fr.
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(13), 1709-1712
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB Substituted biphenyls were prepared and evaluated for their binding affinity for the estrogen receptor. Some of them demonstrated binding better than or equivalent to that of estradiol.

RX(24) OF 53

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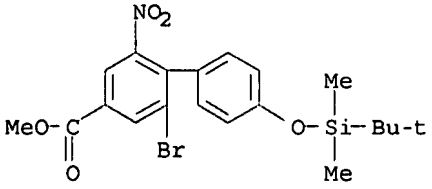
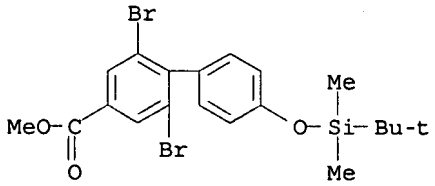
RX(27) OF 53



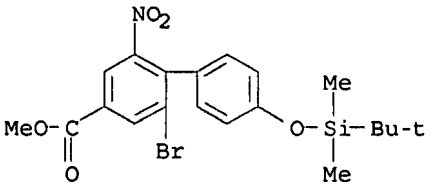

(step 1)

1. Pd(OH)2, Cyclohexene
2. R:594-70-7, CHBr3, CHCl3

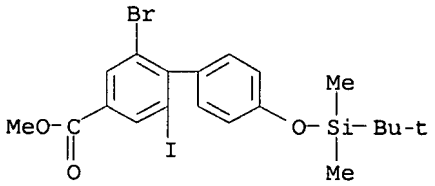



69%

RX(35) OF 53 - 2 STEPS




1. Pd(OH)2, Cyclohexene
2. H2SO4, NaNO2, KI




64%

RETABLE

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| Fanta, P | 1974 | 1 | 9 | Synthesis | |
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| Morgan, L | 1989 | 46 | 3973 | FASEB J | |
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| Nique, F | 1999 | 50 | 21 | J Steroid Biochem Mo | |
| Oh-E, T | 1990 | 4 | 221 | Synlett | |
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L3 ANSWER 6 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 132:78365 CASREACT
TI Preparation of 3-bromo-5-fluorobenzoic acid derivatives
IN Kurumaya, Mitsuo; Honda, Tsunetoshi
PA Tohkem Products Corp., Japan
SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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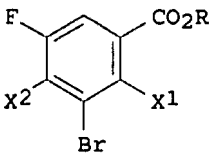
| PI JP2000016971 | A | 20000118 | 1998JP-0180465 | 19980626 |

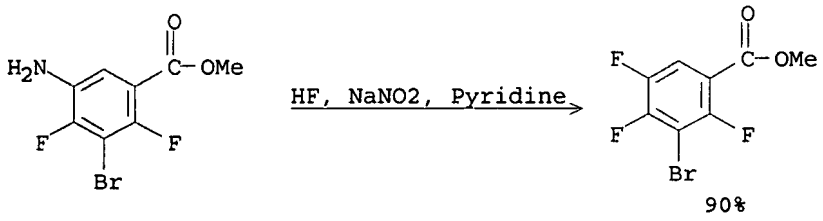
PRAI 1998JP-0180465 19980626
OS MARPAT 132:78365
GI




I

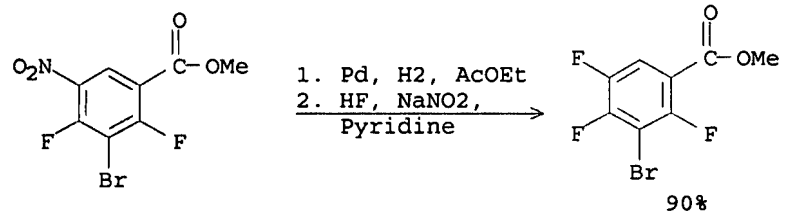
AB Title compds. I (R = H, alkyl; X1, X2 = halo) are prepared by bromination of 2,4-dihalo-5-nitrobenzoic acid derivs. followed by reduction, diazotization, and fluorination. Thus, bromination of Me 2,4-difluoro-5-nitrobenzoate with potassium bromate in 85% H2SO4 gave 68% Me 3-bromo-2,4-difluoro-5-nitrobenzoate, reduction of which with H2 in EtOAc in the presence of 5% Pd/C gave 70% Me 3-bromo-2,4-difluoro-5-aminobenzoate. Diazotization of the latter compound followed by fluorination gave 90% Me 3-bromo-2,4,5-triflurobenzoate.

RX(3) OF 6




NOTE: 2nd step photochem.

RX(5) OF 6 - 2 STEPS

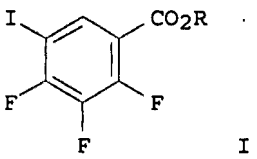



NOTE: 2) 2nd step photochem.

L3 ANSWER 7 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 130:237364 CASREACT
TI Preparation of 2,3,4-trifluoro-5-iodobenzoic acid and its esters
IN Yoneda, Yasuhiro; Yokota, Naoyuki; Ataka, Kikuo
PA Ube Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

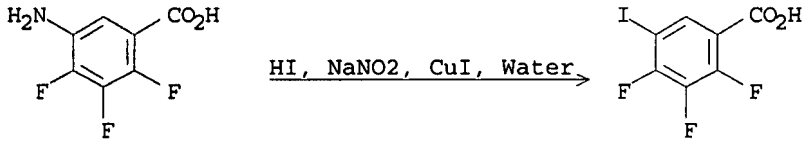
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | JP--11080076 | A | 19990323 | 1997JP-0338495 | 19971209 |
| | JP---3573249 | B2 | 20041006 | | |

PRAI 1997JP-0182766 19970708
OS MARPAT 130:237364
GI



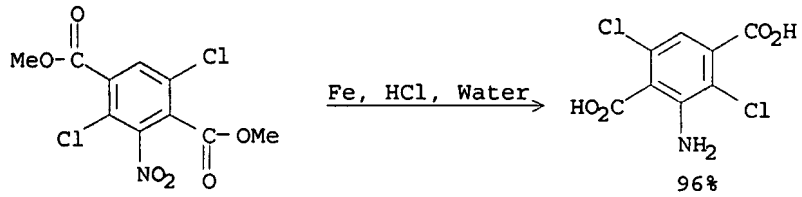

AB Title compds. I (R = H, C1-10 alkyl, C3-10 cycloalkyl, C7-10 aralkyl) were prepared by reaction of 5-amino-2,3,4-trifluorobenzoic acid (II) with HI, alkali metal nitrites, and CuX (X = halo) in solvents. Thus, reaction of II with aqueous HI, CuI, and NaNO2 in H2O gave 2,3,4-trifluoro-5-iodobenzoic acid, refluxing of which with EtOH in toluene in the presence of H2SO4 gave Et 2,3,4-trifluoro-5-iodobenzoate.

RX(1) OF 1




L3 ANSWER 8 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 117:69511 CASREACT
TI Preparation of 2,5-dichloro-3-aminobenzoic acid
AU Yazlovitskii, A. V.; Ral'chuk, I. A.; Shcherbina, F. F.; Grigor'ev, A. A.
CS Inst. Bioorg. Khim. Neftekhim., Kiev, Ukraine
SO Zhurnal Prikladnoi Khimii (Sankt-Peterburg, Russian Federation) (1991), 64(10), 2201-2
CODEN: ZPKHAB; ISSN: 0044-4618
DT Journal
LA Russian
AB Refluxing 2,5,3,6-Cl2(MeO2C)2C6HNO2 with Fe shavings and concentrated HCl in Et2O gave 96% 2,5,3,6-Cl2(HO2C)2C6HNH2, which was decarboxylated by addnl. reflux in 1:1 H2O-concentrated HCl to give 95% title compound

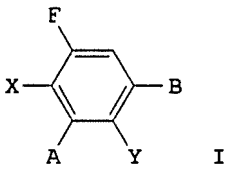
RX(1) OF 3




L3 ANSWER 9 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 116:193920 CASREACT
TI Preparation of fluorobenzoic acids as antibacterial intermediates
IN Kumai, Seisaku; Seki, Takashi; Wada, Akihiro
PA Asahi Glass Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI JP--03275647 | A | 19911206 | 1990JP-0075534 | 19900327 |
| PRAI 1990JP-0075534 | 19900327 | | | |

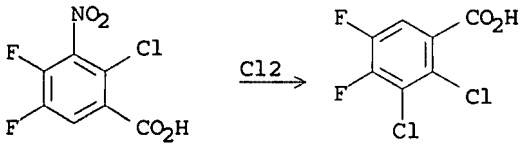
OS MARPAT 116:193920
GI



I

AB The title compds. I (A = Y = Cl, B = CO2H, X = F or Cl), useful as antibacterial intermediates, are prepared by Friedel-Crafts acylation of I (A = B = H, Y = Cl), haloform reaction of I (A = H, B = Ac, Y = Cl), nitration of I (A = H, B = CO2H, Y = Cl), and chlorination of I (A = NO2, B = CO2H, Y = Cl) with chlorinating agents. The title compds. I (A = Cl, B = CO2H, X = F, Y = F or Cl) are prepared by chlorination of I (A = X = Y = Cl, B = CO2H), fluorination of I (A = X = Y = Cl, B = COCl), and hydrolysis of I (A = Cl, B = COF, X = F, Y = F, Cl). Friedel-Crafts acylation of 3,4-difluorochlorobenzene with AcCl and AlCl3 gave 74% I (A = H, B = Ac, X = F, Y = Cl) which was subjected to a haloform reaction to give 85.3% I (A = H, B = CO2H, X = F, Y = Cl) (II). Nitration of II by H2SO4-HNO3 mixture gave 54% I (A = NO2, B = CO2H, X = F, Y = Cl) which was chlorinated by Cl to give 80% I (A = Y = Cl, B = CO2H, X = F).

RX(4) OF 10

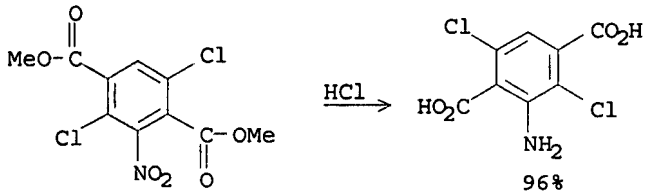


L3 ANSWER 10 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 113:97198 CASREACT
TI Preparation of 2,5-dichloro-3-aminobenzoic acid
IN Ral'chuk, I. A.; Yazlovitskii, A. V.; Shcherbina, F. F.; Grigor'ev, A. A.
PA Institute of Physical-Organic Chemistry and Coal Chemistry, Kiev, USSR
SO U.S.S.R.
From: Otkrytiya, Izobret. 1990, (10), 104.
CODEN: URXXAF
DT Patent
LA Russian
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| SU---1549947 | A1 | 19900315 | 1988SU-4427546 | 19880519 |

PRAI 1988SU-4427546 19880519
AB The title compound was prepared by reduction of di-Me 2,5-dichloro-3-nitroterephthalate by Fe in HCl followed by decarboxylation of the diacid.

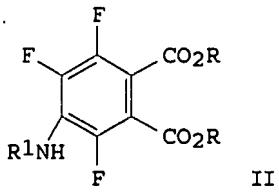
RX(2) OF 3



L3 ANSWER 11 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 112:216450 CASREACT
TI Synthesis of 3-chloro-2,4,5-trifluorobenzoic acid as intermediate for antibacterial agents
IN Wemple, James N.; Karrick, Gregory L.; Spence, Floyd G.
PA Warner-Lambert Co., USA
SO U.S., 7 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US---4885386 | A | 19891205 | 1988US-0264296 | 19881028 |
| CA---1313883 | C | 19930223 | 1989CA-0613205 | 19890926 |
| DK---8905377 | A | 19900429 | 1989DK-0005377 | 19891027 |
| EP----366149 | A1 | 19900502 | 1989EP-0120030 | 19891027 |
| EP----366149 | B1 | 19930113 | | |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| JP--02178254 | A | 19900711 | 1989JP-0278761 | 19891027 |
| JP---2886908 | B2 | 19990426 | | |
| AT-----84518 | T | 19930115 | 1989AT-0120030 | 19891027 |
| ES---2053908 | T3 | 19940801 | 1989ES-0120030 | 19891027 |

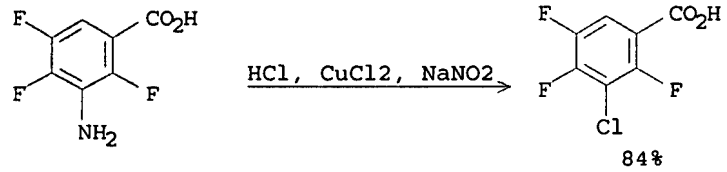
PRAI 1988US-0264296 19881028
1989EP-0120030 19891027
OS MARPAT 112:216450
GI




II

AB The title compound (I), useful as intermediate for quinolone antibacterial agents, was prepared from benzenedicarboxylates II (R = alkyl; R1 = tert-Bu, PhCH2, etc.). A mixture of 4-[(1,1-dimethylpropyl)amino]-3,5,6-trifluoro-1,2-benzenedicarboxylic acid di-Me ester and 36% aqueous HCl was refluxed for 20 h to give 3-amino-2,4,5-trifluorobenzoic acid, which was treated with NaNO2 and CuCl2 in aqueous HCl to give I.

RX(1) OF 2

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L3 ANSWER 12 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 109:230824 CASREACT
TI 8-Cyano-1-cyclopropylquinolonecarboxylic acids as antibacterial agents
IN Schriewer, Michael; Grohe, Klaus; Petersen, Uwe; Haller, Ingo; Metzger, Karl Georg; Endermann, Rainer; Zeiler, Hans Joachim

PA Bayer A.-G., Fed. Rep. Ger.
SO Ger. Offen., 20 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | DE---3702393 | A1 | 19880811 | 1987DE-3702393 | 19870128 |
| | US---4908366 | A | 19900313 | 1988US-0144884 | 19880114 |
| | EP----276700 | A1 | 19880803 | 1988EP-0100503 | 19880115 |
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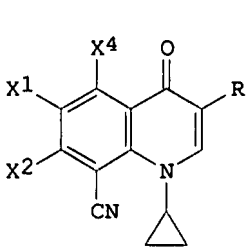
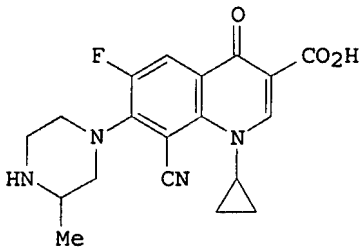
| | CA---1314544 | C | 19930316 | 1988CA-0557311 | 19880126 |
| | JP--63201170 | A | 19880819 | 1988JP-0014771 | 19880127 |
| | US---5051418 | A | 19910924 | 1989US-0434666 | 19891113 |
| | US---5190955 | A | 19930302 | 1991US-0645751 | 19910125 |
| PRAI | 1987DE-3702393 | 19870128 | | | |
| | 1988US-0144884 | 19880114 | | | |
| | 1989US-0434666 | 19891113 | | | |

OS MARPAT 109:230824
GI




I

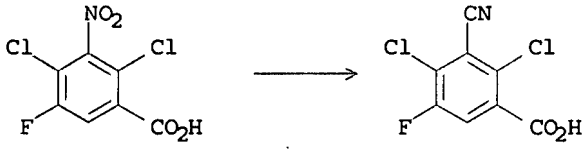



III

AB The title compds. [I; R = CO2H, cyano, CO2R1, CONR2R3; R1 = alkyl; R2 = H, alkyl; R3 = R2, (un)substituted Ph; X1 = H, NO2, alkyl, halo; X2 = heterocyclyl; X4 = H, halo, alkyl] were prepared as antibacterial agents (no data). 2,4,5,3-Cl2F(NC)C6HCOCH2CO2Et (preparation given) was heated 2 h at 150° with HC(OEt)3 in Ac2O to give 2,4,5,3-Cl2F(NC)C6HCOC(:CHR4)CO2Et (II; R4 = OEt) which was stirred 2 h with cyclopropylamine in EtOH to give II (R = cyclopropylamino). The latter was stirred 24 h in dioxane containing KOCMe3 to give, after saponification, I (R = CO2H, X1 = F, X2 = Cl, X4 = H) which was heated 3 h in dioxane with 2-methylpiperazine to give title compound III. Tablets were prepared each containing III 583.0, cellulose 55.0, starch 72.0, polyvinylpyrrolidone 30.0, silica 5.0, and Mg stearate 5.0 mg coated with poly(O-hydroxypropyl-O-methyl)cellulose 6.0, Macrogol 4000 2.0, TiO2 2.0 mg, and polyethyleneglycol (no amount given).

RX(3) OF 15

RX(7) OF 15 - 2 STEPS



L3 ANSWER 13 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 109:73145 CASREACT
TI Process for preparing benzoic acid derivatives useful as antibacterial intermediates
IN Petersen, Uwe; Schriewer, Michael; Kysela, Ernst; Grohe, Klaus
PA Bayer A.-G., Fed. Rep. Ger.
SO Ger. Offen., 11 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | DE---3631906 | A1 | 19880331 | 1986DE-3631906 | 19860919 |
| | US---4851160 | A | 19890725 | 1987US-0090888 | 19870828 |
| | NO---8703689 | A | 19880321 | 1987NO-0003689 | 19870903 |
| | NO----166785 | B | 19910527 | | |
| | NO----166785 | C | 19910904 | | |
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| | EP----266512 | A3 | 19890503 | | |
| | EP----266512 | B1 | 19911204 | | |
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| | AT-----70045 | T | 19911215 | 1987AT-0113034 | 19870907 |
| | ES---2044886 | T3 | 19940116 | 1987ES-0113034 | 19870907 |
| | AU---8778290 | A | 19880324 | 1987AU-0078290 | 19870911 |
| | AU----600020 | B2 | 19900802 | | |
| | IL-----83919 | A | 19910630 | 1987IL-0083919 | 19870916 |
| | FI---8704063 | A | 19880320 | 1987FI-0004063 | 19870917 |
| | FI-----86843 | B | 19920715 | | |
| | FI-----86843 | C | 19921026 | | |
| | DD----269146 | A5 | 19890621 | 1987DD-0307030 | 19870917 |
| | CA---1325018 | C | 19931207 | 1987CA-0547091 | 19870917 |
| | DK---8704902 | A | 19880320 | 1987DK-0004902 | 19870918 |
| | DK----168212 | B1 | 19940228 | | |
| | JP--63088157 | A | 19880419 | 1987JP-0232702 | 19870918 |
| | JP--05076934 | B | 19931025 | | |
| | ZA---8707027 | A | 19880525 | 1987ZA-0007027 | 19870918 |
| | HU-----45001 | A2 | 19880530 | 1987HU-0004174 | 19870918 |
| | HU----197872 | B | 19890628 | | |
| | CN--87106482 | A | 19880330 | 1987CN-0106482 | 19870919 |
| | CN---1024415 | B | 19940504 | | |
| | US---4990661 | A | 19910205 | 1989US-0330396 | 19890329 |
| | JP--06025125 | A | 19940201 | 1993JP-0124640 | 19930430 |
| | JP--06094446 | B | 19941124 | | |
| | DK---9300861 | A | 19930721 | 1993DK-0000861 | 19930721 |
| | DK----170253 | B1 | 19950717 | | |

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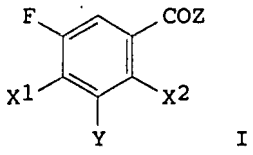
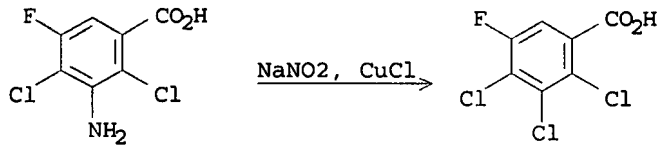
1987US-0090888 19870828
1987EP-0113034 19870907
OS MARPAT 109:73145
GI



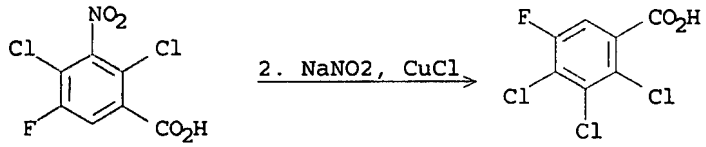
I

AB Title compds. I (X1, X2 = F, Cl; Y = F, Cl, Br, iodo; Z = F, Cl, OH), useful as antibacterial intermediates, are prepared Diazotization of 3-amino-2,4-dichloro-5-fluorobenzoic acid and treatment with CuCl gave 94% I (Z = OH, X1, X2, Y = Cl).

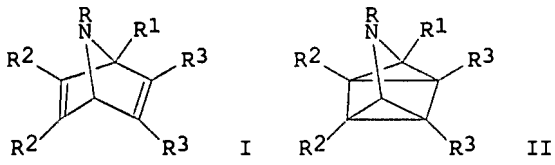
RX(4) OF 21



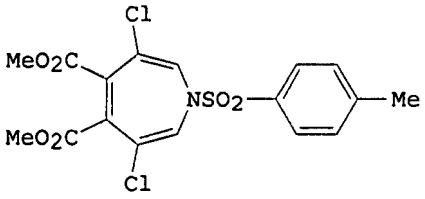

RX(8) OF 21 - 2 STEPS




L3 ANSWER 14 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 105:24171 CASREACT
TI Photochemical transformations. 65. The 3σ → 3π-route to 1H-azepines/benzene imines
AU Prinzbach, Horst; Bingmann, Horst; Fritz, Hans; Markert, Juergen; Knothe, Lothar; Eberbach, Wolfgang; Brokatzky-Geiger, Juergen; Sekutowski, Janine C.; Krueger, Carl
CS Chem. Lab., Univ. Freiburg, Freiburg/Br., D-7800, Fed. Rep. Ger.
SO Chemische Berichte (1986), 119(2), 616-44
CODEN: CHBEAM; ISSN: 0009-2940
DT Journal
LA German
GI



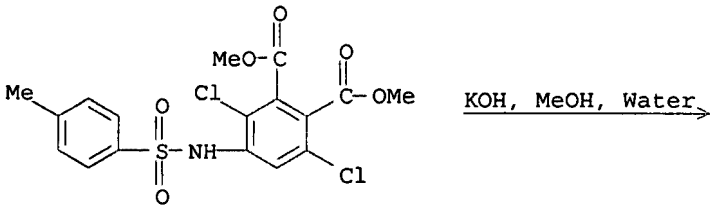
I II

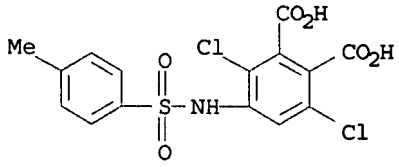


III

AB With several newly prepared substrates the influence of substituents upon the individual steps in the 3σ→3π-route to 1H-azepines is more precisely defined. The 7-azanorbornadienes I (R = tosyl, CO2CH2CH:CH2; R1 = H, CH2OCH2C.tplbond.CH; R2 = H, Cl; R3 = H, CO2Me) are selectively isomerized by sensitized or direct photoexcitation into the azaquadricyclanes II, some of which are highly unstable. For the thermal conversion of II (R = tosyl, R1 = R3 = H) the kinetic parameters have been determined (benzene); Ea = 28.0 ± 0.2 kcal/mol, lg A = 15.7; ΔH.thermod. = 27.3 ± 0.2 kcal/mol, ΔS.thermod. = 1.1 ± 0.7 e.u. This barrier is lowered more efficiently in II (R2 = Cl) than in II (R3 = CO2Me) with the former and latter causing exclusive scission of the opposite and neighboring cyclopropane bonds resp. The intermediate azomethine ylides are captured with dipolarog. reagents more or less efficiently depending on their substitution pattern. In II (R = tosyl, R1 = CH2OCH2C.tplbond.CH, R2 = H, R3 = CO2Me) the intramol. addition of the unactivated yne component at -30° is so fast, that azepine formation is almost totally suppressed. The azepinebenzeneimine equilibrium mixture from II (R = tosyl, R1 = H, R2 = Cl, R3 = CO2Me) (.apprx.9:1) crystallizes as the azepine III (x-ray crystal structure anal.).

RX(30) OF 135



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